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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/889,251	11/01/2001	Robert K. Naviaux	UCSD1140-1	9760

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EXAMINER	
SPIVACK, PHYLLIS G	
ART UNIT	**PAPER NUMBER**
1614	

DATE MAILED: 09/13/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/889,251	NAVIAUX, ROBERT K.	
	Examiner	Art Unit	
	Phyllis G. Spivack	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 August 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *67,70,73-91 and 95* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *95* is/are allowed.

6)☒ Claim(s) *67,70 and 73-91* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8-12-05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Applicant's Reply and Terminal Disclaimer filed August 12, 2005 are acknowledged. New claim 95 is presented. Accordingly, claims 67, 70, 73-91 and 95 are now under consideration.

An Information Disclosure Statement filed August 12, 2005 is further acknowledged. All references have been considered.

The indication of finality set forth in the last Office Action is withdrawn.

In the last Office Action claims 67-80 and 88-91 were rejected under 35 U.S.C. 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to enable one skilled in the art to practice the invention. The claims are directed to the treatment of mitochondrial disorders comprising administering uridine or 1-β-D-ribofuranosyluracil. The specification provides support for the treatment of MARIAHS syndrome comprising administering uridine in Example 2. All other exemplifications comprise administering triacetyluridine.

Applicant argues the specification complies with the enablement requirement in that no undue burden is needed to practice the present methods. Examples are provided showing what compound is to be used along with dosing requirements. Further, Applicant urges the Examples are non-limiting and are merely illustrative and the teachings apply to both triacetyluridine and uridine.

Applicant's arguments are persuasive with respect to claims 67, 70, 73, 75, 82 and 83; the rejection of record under 35 U.S.C. 112, first paragraph, is withdrawn. The rejection is, however, maintained over claims 74, 76-79, 82 and 83 for the reasons of

record. The specification is silent concerning the administration of drugs for the treatment of AIDS, a deficiency of cardiolipin and lower than normal uridine levels.

The rejection of record under 35 U.S.C. 112, second paragraph, is withdrawn following the deletion of the term "general" in claims 67 and 91.

Subsequent to the filing of a Terminal Disclaimer, the provisional rejection of the claims under the judicially created doctrine of obviousness-type double patenting is withdrawn.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 67, 70, 73-91 are rejected under 35 U.S.C. 103(a) as being unpatentable over Page et al., Proc. Natl. Acad. Sci., in view of von Borstel et al., U.S. Patent 6,472,378.

Page teaches the administration of uridine to treat developmental disorders accompanied by seizures, ataxia, recurrent infections, severe language deficit, and an unusual behavioral phenotype characterized by hyperactivity, short attention span and poor social interaction. See the Abstract. Patients were treated with 50-1000 mg/kg/day, a dosage range that overlaps with those required by claims 88-90. See column 2, page 11604. The claims differ in that Page fails to use the recitation "mitochondrial disorder". However, von Borstel teaches the administration of uridine, an example of a "pyrimidine nucleoside precursor", to treat a variety of clinical disorders

secondary to mitochondrial dysfunction that include neurodevelopmental delays, age-related neurodegenerative diseases, as well as multiple pathologies involving diverse organ systems. See column 4 and, in particular, column 14, under Treatment of Developmental Delay. Congenital genetic deficiencies and acquired deficiencies in the activity of one or more components of the mitochondrial respiratory chain are encompassed in the disclosure. As required by instant claims 67 and 91, renal tubular acidosis, multiple mitochondrial deletion syndrome, Leigh syndrome, lactic academia, encephalomyopathy, complex I deficiency, complex IV deficiency and ataxia are among the disorders discussed in the reference. Further, congenital mitochondrial diseases related to hereditary mutations are disclosed in column 4, lines 10-15 and at the top of column 10. As required by claim 73, a mitochondrial disorder may be secondary to an infection, including a viral infection. See column 12, line 39. As required by claim 75, the mitochondrial disorder comprises a deficiency in a pyrimidine synthetic pathway. See column 4, lines 48-59. As required by claims 80, 81 and 84, the mitochondrial disorder is the result of prior or concurrent administration of a pharmaceutical agent, such as Brequinar. See column 11, line 32. As required by claims 85-87, the methods of treatment may further comprise the administration of co-factors and vitamins, such as CoQ10, B vitamins and lipoic acid. See column 12, lines 53-54.

It would have been obvious to one of ordinary skill in the art at the time of the invention to treat patients having a mitochondrial disease with uridine in view of the combined teachings of the prior art. Although the term "mitochondrial disorder" was not disclosed in the teachings of Page, von Borstel teaches the administration of uridine for

the treatment of a variety of disorders, syndromes and conditions involving diverse organ systems wherein mitochondrial dysfunction contributes to or causes the pathology. The combined teachings of the prior art would have motivate one skilled in the art to administer uridine in the treatment of the various developmental disorders accompanied by seizures, ataxia, recurrent infections, severe language deficit, and an unusual behavioral phenotype characterized by hyperactivity, short attention span and poor social interaction that are disclosed by Page, the same or similar disorders taught by von Borstel to be of dysfunctional mitochondrial origin. As clarified by Applicant in the Reply filed August 12, 2005, there is a close relationship between triacetyluridine and uridine. Since the instant specification provides enough guidance with respect to triacetyluridine, using uridine would require no more than minor variations in the practice of the invention. Further, acyl derivatives of uridine have better oral bioavailability.

Claim 95 is free of the prior art.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Phyllis G. Spivack whose telephone number is 571-272-0585. The Examiner can normally be reached from 10:30 to 7 PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Christopher Low, can be reached 571-272-951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Phyllis Spivack

September 8, 2005

Phyllis Spivack
1614

PHYLLIS SPIVACK
PRIMARY EXAMINER